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EXAMINER

WOITACH, JOSEPH T

ART UNIT

PAPER NUMBER

1632

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16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/527,026

Applicant(s)

WEST ET AL.

Examiner

Joseph Weitach

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 May 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 69-231 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 69-231 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s) _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

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DETAILED ACTION

This an original application filed March 16, 2000, which claims benefit to provisional applications; 60/179,486, filed February 1, 2000, and 60/152,340, filed September 7, 1999.

Applicants preliminary amendment filed April 11, 2002, paper number 12, has been received and entered. The specification has been amended. Claims 3, 17 and 18 have been canceled. Claims 1, 4, 7, 13, 21, 22, 25, 29, 37 and 39 have been amended. Additionally, Applicants amendment filed May 28, 2002, paper number 15, has been received and entered. The specification has been amended. Claims 1, 2, 4-16, and 19-68 have been canceled. Claims 69-231 have been entered. Claims 69-231 are pending and currently under examination.

Oath/Declaration

The substitute declaration filed May 28, 2002, paper number 14 is in compliance with 37 CFR 1.67(a). The objection to the declaration is withdrawn.

Specification

The objection to the disclosure because the specification contained several references to a URL is withdrawn.

Amendments to the specification has obviated the basis of the objection.

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Claim Objections

Claim 69, 106, 113, 128, 136 and 151 are objected to because of the following informalities: The claim includes internal periods. Each claim must begin with a capital letter and end with a period. See MPEP 608.01(m). Specifically, each of the numbered steps contain periods. Amending the claim to include parenthesis instead of periods would obviate the basis of the rejection.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 197 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

In the instant case, the recitation of "the genome of which is of a species different than that of the mitochondria of the cells" is considered new matter. A review of Applicants' summary of the new claims, it is noted that support for claim 197 is not specifically set forth in

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Applicants summary. Examiner notes that this recitation was not present in the previous claims, and upon review of the present specification Examiner could not find literal support for this recited claim amendment. The specification does not teach any specific characteristics of the mitochondria of the starting cell nor the resulting cell.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claim 197 is also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to

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determine whether or not “new matter” is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure*” (emphasis added).

Claims 69-231 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of providing primary cells comprising: a) enucleating an oocyte of a first mammalian species and transferring the nucleus of a primary cell from the same species as the recipient oocyte into said oocyte; b) activating the NT unit; c) culturing the activated NT unit in a immunocomprimized mouse to produce a teratoma; and d) isolating a differentiated cell from said teratoma, and cells derived by said method, does not reasonably provide enablement for use of any source of host cell from a first species, nor the use of any organism besides a mammalian species.

Cancellation of the claims has obviated the basis of the previous rejection. Further, it is noted that newly added claims encompass specific embodiments which were indicated as enabled in the basis of the previous rejection. However, it is noted that newly added claims encompass cross-species nuclear transfer, as specifically set forth in claims 83 and 166, and implicitly set forth in claim 197. The newly amended claims are drawn to a method of nuclear transfer wherein the resulting cell derived from an embryo is a rejuvenated primary cell. The basis of the rejection is directed towards the breadth encompassed by the specific method step of using a nuclear donor and an oocyte from two different and unrelated species. The art supports that the donor nucleus is reprogrammed by yet unknown components of the recipient cytoplasm where

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the donor nucleus is reverted to the same morphological and temporal pattern of the zygote. Further, the art indicates that while the nucleus of one species can be physically transferred into the oocyte of second different species, the resulting chimeric embryo is incapable of supporting the proliferation of said embryo. Depending on the phylogenetic distance of the two species used in the nuclear transfer method, after several rounds of division the cells in the chimeric embryo cease to proliferate, thus cross-species nuclear transfer can not result in a rejuvenated cell. Because the instant application relies on the teachings known in the art of nuclear transfer, Examiner would agree that the examples recited in the instant specification are enabled by the methodology commonly practiced in the art. The newly added claims are not limited to these enabled embodiments, in particular the claims encompass cross-species nuclear transfer. In light of Applicant's reliance on the art for practice of the claimed process and resulting cell, the instant specification and the art of record fails to provide the necessary guidance which would enable the artisan to practice the invention commensurate in scope as instantly claimed.

As noted in the previous office action, the detailed description of the invention, it is stated that the invention provides a method for rejuvenating primary cells through nuclear transfer techniques. The instant invention is drawn from Applicants' observation that practicing nuclear transfer methods, that a donor cell nucleus can be reprogrammed to become a pluripotent cell when transferred into an oocyte and properly cultured. However, the specification fails to teach how the art taught and practiced methods of nuclear transfer differ from those instantly claimed. The specification clearly indicate the reliance of the art to practice the instant invention, and thus,

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the only working embodiments which are enabled are those specifically supported by the art.

Lacking the necessary guidance, the specification fails to provide a nexus between art recognized limitations and the ability to practice the full scope of the invention as presently claimed.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and the state of the art at the time of the claimed invention was made, it would have required one of skill in the art undue experimentation to practice the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Cancellation of the claims has obviated the basis of the previous rejections.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 69-231 are rejected under 35 U.S.C. 102(a/e) as being anticipated by Strelchenko *et al.* (US Patent 6,011,197) or Damiani *et al.* (US Patent 6,258,988) as further evidenced by Evans *et al.* (Nature Genetics 23:90-93).

First, Applicants note that the teaching of Evans *et al.* is directed to mitochondrial DNA content of a cell after nuclear transfer, and is not directed to rejuvenating a cell by nuclear transfer. Focusing on Strelchenko *et al.* (US Patent 6,011,197) or Damiani *et al.*, Applicants summarize the teachings of the cited references and note that none of the references teach that the methods result in a rejuvenated cell with increased proliferation life-span and restored telomeres. Applicants note that at the time of filing the prior art teaches away from the instant invention. Discussing Shiels *et al.* Applicants note that the use of nuclear transfer to generate the cloned sheep Dolly resulted in an animal with telomeres just as short as those from the donor cell used to clone her. Further, it is argued that the findings of Shiels *et al.* would call into question the extent of genetic manipulation that may be performed when using somatic cell transfer. Applicants argue that prior to the teaching in the prior disclosure the skilled artisan would have expected that practicing nuclear transfer that the resulting cell would have telomeres the same length as the donor. The present invention goes directly against this view and demonstrates that

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practicing the instantly claimed invention represents surprising and unexpected results. See Applicants' amendment filed April 11, 2002 paper number 12, pages 15-20. Applicants' arguments have been fully considered but not found persuasive.

Newly added claims 87-210 encompass a method for rejuvenating a cell and making a primary cell by the use of nuclear transfer technology. In light of the teachings of the instant specification and the specific steps recited in instant claims, the method is drawn to the use of nuclear transfer methods to generate a primary cell. The ability to provide a differentiated cell encompasses methodology of nuclear transfer and isolation of a differentiated cell from a teratoma. Claims are also drawn to genetically modifying the rejuvenated cell. Additionally, it should be noted that claim 197 is directed to a resulting cell "the genome of which is of a species different than that of the mitochondria of the cells".

First, it should be noted that the broadest claims are drawn to generating a rejuvenated cell. Clearly using nuclear transfer results in a rejuvenated cell considering that a primary cell does not have the capacity that the resulting embryo does in generating a complete animal. Further, transplanting the primary cell does not result in the formation of a teratoma from which cell type from each of the three germ layers can be identified. As noted in the specification and Applicants' arguments the present invention is based on the unexpected observation that nuclear transfer results in a cell with increased telomere length, however there is no argument to the fact that the present invention relies on art enabled embodiments of nuclear transfer and that the methods as instantly claimed provide no novel steps not disclosed in Strelchenko *et al.* or

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Dimiani *et al.* As summarized in the previous office action, Strelchenko *et al.* teach a method of nuclear transfer wherein the resulting cell is used in methods to clone a bovine, and Dimiani *et al.* teach a method of nuclear transfer wherein the resulting cell is used in methods to clone an ovine. Both, Strelchenko *et al.* and Dimiani *et al.* teach that the methodology can be used to generate an animal in which a heterologous sequence is introduced. The specification relies on the methods taught in the art for the practice of the claimed invention, and the instant claims recite the same method steps known in the art of nuclear transfer, and thus practicing the methods known in the art as taught by Strelchenko *et al.* and Dimiani *et al.* would inherently result in cells with the observed phenotype. Additionally, Evans *et al.* teach that practicing the methodology of nuclear transfer, the resulting cell may contain the mitochondria of the oocyte, rather than the donor cell. The instant claims are not distinguished from nuclear transfer methods known in the art by simply providing a new description of the resulting product or reciting a new intended use in the preamble of claim which encompasses methodology previously disclosed in the art. As noted in the previous office action, when, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product (*In re Ludtke*). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re*

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Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). In the instant case, Applicants have not argued that the presently claimed method steps differ from those disclosed in *Strelchenko et al.* and *Dimiani et al.*, only that the result of practicing the method would result in a cell with a phenotype not previously described. Thus, the methods taught in *Strelchenko et al.* and *Dimiani et al.* anticipate the instantly claimed methods and cells produced by said method.

Claims 69-231 are rejected under 35 U.S.C. 102(b) as being anticipated by *Robl et al.* (WO 98/07841) as evidenced by *Evans et al.* (Nature Genetics 23:90-93).

Applicants argue that *Robl et al.* does not disclose increased telomere length, and as argued above for *Strelchenko et al.* and *Dimiani et al.* does not anticipate the instantly claimed invention. See Applicants' amendment filed May 11, 2002, paper number 12, pages 20-21. Applicants' arguments have been fully considered but not found persuasive.

The newly added claims are summarized above. *Robl et al.* teach a method of cross-species nuclear transfer wherein the resulting cell is chimeric cell comprising an enucleated oocyte which is different from that of the transferred nuclei. As argued above, because the specification relies on the methods taught in the art for the practice of the claimed invention, and since practicing the method of nuclear transfer would inherently result in the cells presently claimed, the methods and resulting cells taught in *Robl et al.* anticipate the claims as they are drawn to generating a modified cell. Because the claimed and prior art products are identical or

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substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product (*In re Ludtke*). Further, whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). In the instant case, it is unclear how the instantly claimed methods and the resulting cells from said methods are materially different from the methods of nuclear transfer known and taught in the art, and thus, the methods taught in Robl *et al.* anticipate the instantly claimed methods and cells produced by said method.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Newly added claims 69-231 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 87-210 of copending Application No. 09/250,879. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Newly added claims 69-231 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 69-231 of copending Application No. 09/656,173. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

In the instant case, it is noted that the claims of the instant application have been added, however the subject matter of the instant claims and the pending claims of 09/250,879 and 09/656,173 are drawn to the same invention. Specifically, each invention is drawn to a method of generating a rejuvenated cell through nuclear transfer techniques.

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Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached at (703)305-4081.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

Deborah Crouch
DEBORAH CROUCH
PRIMARY EXAMINER
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